

REMARKS

Claims 1, 2, 4, 5, 22, 24-28, 34 and 35 constitute the pending claims in the present application. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1. Applicants note with appreciation that the amendments filed March 24, 2003 have been entered. Claims 1, 2, 4, 5, 22, 24-28, 34 and 35 are pending and under examination.
2. Applicants note with appreciation that the rejection of the claims under 35 U.S.C. 112, first paragraph, has been withdrawn.
3. Applicants note with appreciation that the rejection of the claims under 35 U.S.C. 103(a) as allegedly unpatentable over Fujitsa et al. has been withdrawn. However, the Examiner alleges that although the previously entered amendments overcome this rejection, they introduce new matter which must be deleted to overcome a new matter objection under 35 U.S.C. 132 and a rejection under 35 U.S.C. 112, first paragraph, which have been newly applied in this Office Action. The Examiner further alleges that amendments to the claims to obviate the new matter objection and rejection would result in reinstatement of the rejection under 35 U.S.C. 103(a).

Applicants will present in detail below arguments specific to the new matter rejection. However, Applicants respectfully submit for the record that the amendments and arguments presented in this response will satisfy all of the conditions for patentability including the requirements under 35 U.S.C. 103(a). Applicants respectfully remind the Examiner that the standard for anticipating a claim is outlined in MPEP 2131, and is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). "The identical invention must be shown in as complete detail as is contained in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

As previously pointed out, Fujita et al. fail to teach a method for inhibiting proliferation and growth of lung cancer tissue by influencing the mesenchymal cells which surround the lung

cancer tissue, as set forth in the claims (i.e., by decreasing hedgehog signaling in the mesenchymal cells). In fact, the in vitro system employed by Fujita et al. would not even have allowed the investigators to assess whether administration of hedgehog antibodies would result in decreased expression of hedgehog in the surrounding mesenchymal tissue. Additionally, as previously pointed out by Applicants, Fujita et al. fail to teach in vivo methods for inhibiting growth of lung cancer tissue. Accordingly, Fujita et al. fail to satisfy the criteria for anticipating the claimed subject matter, and Applicants respectfully submit that the rejection under 35 U.S.C. 103(a) was rightfully withdrawn and should not be reapplied.

4-5. The amendment filed March 24, 2003 is objected to under 35 U.S.C. 132 as allegedly introducing new matter into the disclosure, and claims 1, 2, 4, 5 and 24-28 are rejected under 35 U.S.C. 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to convey to one of skill in the art that Applicants had possession of the claimed invention. This rejection under 35 U.S.C. 112, first paragraph, is a new matter rejection. Applicants traverse both the objection and rejection and contend that they are moot in light of the amended claims.

In assessing compliance with 35 U.S.C. 112, first paragraph, the “fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed.” (MPEP 2163; See also, e.g., *Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117). Applicants maintains that the previously filed amendments satisfied this requirement. Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to more particularly point out certain embodiments of Applicants’ invention. Applicants’ amendments are not in acquiescence of the objection or rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

Applicants direct the Examiner’s attention to the following passages of the specification which provide support for the claimed subject matter: page 3, line 25 – page 4, line 2; page 9, lines 8-11; page 10, lines 3-6; page 11, lines 10-12; page 70, line 26 – page 71, line 4; page 71, lines 27-29; and page 73, lines 1-4. Applicants note that these passages are provided merely to

exemplify the extensive support found in the application for the claimed subject matter, and are not intended to be limiting or to provide an exhaustive inventory of supporting passages.

“The interaction of a *hedgehog* protein with one of its cognate receptor, *patched*, sets in motion a cascade involving the activation and inhibition of downstream effectors, the ultimate consequence of which is, in some instances, a detectable change in the transcription or translation of a gene. Transcriptional targets of hedgehog signaling are the *patched* gene itself and the vertebrate homologs of the drosophila cubitus interruptus (Ci) gene, the *GLI* genes. *Patched* gene expression has been shown to be induced in cells of the limb bud and the neural plate that are responsive to *Shh*.” (page 3, line 25 – page 4, line 2)

“Mesenchyme differentiation at 18.5 dpc. (a) Both wt and mutant lungs display cartilaginous rings around the trachea as indicated by alcian-blue staining. (b) While in the wild-type lung a layer of smooth muscle surrounds the conducting epithelium, the mutant lung mesenchyme does not differentiate into muscle.” (page 9, lines 8-11 – figure legend for Figure 3)

“These results highlight the importance of epithelially derived Shh in regulating branching morphogenesis of the lung, and establish a role for *hedgehog* in lung morphogenesis, disease and repair, and suggest that SHH normally regulates lung mesenchymal cell proliferation *in vivo*.” (page 10, lines 3-6)

“Our observations set forth below reveal potential new roles for the *hedgehog/patched* pathway in maintenance of proliferation and differentiation of lung tissue.” (page 11, lines 10-12)

“*Patched* genes encode proteins thought to be *Hedgehog* receptors, while *Gli*-genes encode transcriptional mediators of *Hedgehog*

signaling. Both *Ptc-1* and *Gli-1* are up-regulated when *Shh* is ectopically expressed in the lung indicating that here, as elsewhere in the embryo, they are transcriptional targets of *Shh* signaling. Consistent with this model, *Ptc-1* and *Gli-1* are normally expressed in the mesenchyme of wild-type embryos with highest levels at the distal branch points mirroring epithelial *Shh* expression. In *Shh* mutants, only basal levels of expression of both genes are detected.” (page 70, line 26 – page 71, line 4)

“This observation lends further support to the model that the lung mesenchyme is the primary target of *Shh* signaling and indicates that mesenchymal signaling is abnormal in *Shh* mutants.” (page 71, lines 27-29)

“They also indicate that the genetic control of growth and branching in the lung epithelium is most likely a complex process involving both epithelial and mesenchymal interactions at the branch points, and that the downstream targets of *Shh* signaling in this organ are primarily mesenchymally expressed genes.” (page 73, lines 1-4)

Applicants contend that the amended claims satisfy all of the requirements under 35 U.S.C. 112, first paragraph, and that no new matter has been entered. In accordance with MPEP 2163, “newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.” Applicants contend that this standard has been met. Applicants additionally note that the prohibition against the addition of new matter does not require that claims find *in haec verbiis* support in the specification (MPEP 2163). In light of Applicants’ amendments and arguments, reconsideration and withdrawal of the objection under 35 U.S.C. 132 and the rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

6. Claims 1, 2, 4, 5 and 24-28 are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to enable one of skill in the art to practice the claimed invention. Applicants traverse this rejection and maintain that the rejection is moot in light of the amended claims.

The basis of the rejection appears to be the Examiner's contention that a hedgehog antibody that binds to hedgehog protein in lung tissue would not alter the expression of hedgehog itself. Firstly, Applicants contend that the Examiner's statement is not necessarily correct. One of skill in the art would readily appreciate that under any of a number of circumstances, an antagonistic antibody that binds to a particular protein would also decrease expression of that protein. By way of example, Applicants cite a protein X involved in promoting signaling via a pathway that normally functions to promote expression of protein X (e.g., a positive feedback loop). Under such relatively common circumstances, an antagonistic antibody that bound to and inhibited the function of protein X would also lead to a decrease in the expression of protein X. Accordingly, Applicants disagree with the general scientific comments made in the prior Office Action with respect to the basis of this rejection.

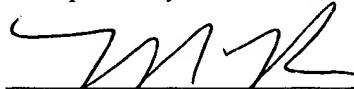
Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to more particularly point out certain embodiments of the invention. Applicants' amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. The amended claims specify that the administration of the hedgehog antibody is effective to decrease **hedgehog signaling** in mesenchymal cells, and this embodiment of the invention is supported by the specification as outlined in detail in sections 4 and 5 above. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this Reply, please charge the fees to our **Deposit Account No. 18-1945**. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit account.

Respectfully Submitted,



Melissa S. Rones
Reg. No. 54,408

Date: August 4, 2003

Customer No: 28120
Docketing Specialist
Ropes & Gray
One International Place
Boston, MA 02110
Phone: 617-951-7000
Fax: 617-951-7050